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May 5, 2003

VIA FACSIMILE (202) 225-1919 & FEDERAL EXPRESS

Hon. W.J. "Billy" Tauzin
Chairman
Committee on Energy and Commerce
U.S. House of Representatives
2183 Rayburn HOB
Washington, D.C. 20515

Dear Rep. Tauzin:

This letter is in response to your letter dated April 21, 2003 relative to the comprehensive review by your committee of safety issues surrounding the use of ephedra-containing dietary supplements.

Background

NVE was founded in 1980 by Robert Occhifinto. Since that time, the company has grown from a small, less than 10 person operation, to its present status as an employer of approximately 100 full time workers. The company is in the midst of a long-planned expansion, at the conclusion of which it anticipates that it will have over 200 full time employees. NVE is presently one of the largest employers in Newton, New Jersey and anticipates that it will be one of the largest employers in Sussex County, New Jersey.

NVE is a member of the American Herbal Products Association ("AHPA") and has undertaken to abide by all of the bylaws and other requirements of that group. As you may know, AHPA is the leading trade organization representing marketers of herbal products in the United States. AHPA is a consistent advocate of the responsible marketing, use, and regulation of herbal products in the United States, and NVE joins wholeheartedly in these objectives as they relate to the industry in general and to the products marketed by NVE in particular. AHPA has also repeatedly called upon the United States Food and Drug Administration ("FDA") to fulfill its obligations with the

law, including promulgating Good Manufacturing Practices and regulations pertaining to the responsible marketing of ephedra-containing products. NVE joins AHPA in this call for promulgating of current Good Manufacturing Practices ("cGMPs") and regulations pertaining to responsible marketing of ephedra-containing products.

Ephedra

The majority of the products marketed by NVE contain the Chinese herb ephedra. This herb has a long history of use, dating back thousands of years. The Chinese specifically recognized ephedra's utility in the alleviation of certain bronchial conditions, as well as its mild stimulant effect. Ephedra has been safely used for thousands of years in Asia, Europe and the Americas for these purposes.

As with any substance that is pharmaceutically active, especially substances with stimulant effects, proper use of ephedra products is essential. Abuse and/or misuse of any stimulant product is inherently risky and should not be encouraged in any way. It is the nature of these substances, however, that unfortunately leads a few misguided or misinformed individuals to believe that consumption of excessive amounts of ephedra-containing products will provide exponentially enhanced effects without consequences. As part of its efforts to address this reality, every ephedra-containing product sold by NVE bears extensive warnings, alerting consumers that consumption of amounts in excess of label directions can pose the risk of severe adverse events. Warnings on NVE products specifically note that abuse can cause stroke and heart attack. NVE respectfully submits that these warnings go well beyond those commonly provided on over-the-counter drugs such as acetaminophen (e.g. Tylenol®) and ibuprofen (e.g. Advil®).

Significantly, the most recent available Drug Abuse Warning Network (DAWN) Final Estimates Report, prepared by the Department of Health and Human Services, Substance Abuse and Mental Health Services Administration, reflects that adverse events associated with acetaminophen are the fourth most common cause of emergency room (ER) admissions in the United States, with over 39,165 occurrences in 2001. Ibuprofen was identified as the cause of 17,123 reported ER admissions during the same year.

On the other hand, DAWN identifies ephedrine (which we include here due to the common misunderstanding associated with the herb ephedra and the OTC drug ephedrine) as the cause of 728 ER admissions in 2001, while the entire category of nutritional products were identified as the cause of 1,449 admissions. This data clearly demonstrates that, whatever the risk associated with ephedra products, it is a mere fraction of that posed by the OTC products mentioned above.

Post-marketing Surveillance

A number of Congressional Representatives have expressed their concerns with post-marketing surveillance activities as they specifically relate to ephedra and to other herbs

and dietary supplements in general. NVE recognizes that this is a proper area for concern and that governmental action in this area is essential. Representatives of AHPA and other industry trade associations specifically addressed these concerns, noting deficiencies in FDA's current Adverse Event Reporting (AER) system at a hearing held by the House Committee on Government Reform on May 27, 1999. At that hearing, FDA agreed that its then operational system was in need of improvement, but suggested that it believed the system was good enough to provide the necessary warnings when unsafe products enter the market.

Unfortunately, while that may have been the case in theory, events have proven the contrary to be true. As noted in a report issued by the General Accounting Office (GAO) on August 4, 1999, FDA's system for accepting and investigating AERs associated with dietary supplements was woefully inadequate and subject to abuse by the Agency. This GAO report dealt with FDA's first effort to promulgate a regulation restricting the sale of ephedra-containing products on the basis of individual dose and daily levels of ingestion. As noted by the GAO, however, this proposed regulation, which the FDA represented was grounded upon hundreds of AERs received by the Agency concerning ephedra, was severely flawed by reliance on bad science.

Specifically, GAO cited FDA's failure to properly analyze many of the AERs reported to it, accepting numerous unfounded claims as the basis for its proposed rule making. Indeed, a specific analysis of a variety of the AERs reported by FDA by our firm indicated that the Agency was attributing virtually any report submitted to it as factual and reliable, no matter how bizarre or regardless of whether the incident involved an expected effect from the herb. For example, our research found the Agency's roster of ephedra related adverse events to include:

A report by a 70 year-old woman that her menstrual cycle had resumed following her use of an ephedra related dietary supplement.

An autopsy report reflecting that the decedent had apparently ingested an ephedra product, while the actual cause of death was a "shotgun blast to the chest."

Numerous reports of sleeplessness in individuals ingesting multiple doses of ephedra shortly before bedtime, or in conjunction with multiple cups of coffee or other caffeinated beverages.

FDA is presently working to revise its AER system for dietary supplements. AHPA is actively engaged in this effort which NVE fully supports.

NVE also recognizes the need for the adoption of standardized procedures for the reporting and handling of AERs within the industry. Toward this end, we respectfully submit that it is incumbent upon FDA to promulgate GMPs for the dietary supplement industry - something it was expressly directed to do as part of the Dietary Supplement

Health and Education Act of 1994. Some nine years later, we have finally been provided with a draft document from FDA. NVE believes that it is significant that, until this document was finally published in February of this year, the only substantive efforts to date in this area have come from the industry itself, specifically the Industry Draft cGMP document submitted to FDA and published in the Federal Register on February 6, 1997. NVE notes that the current draft cGMP regulation published by FDA contains no provision mandating the investigation and reporting of adverse events.

On March 23, 2003, AHPA submitted a Citizen Petition to the FDA urging the Agency to establish, through rulemaking, a requirement for marketers of dietary supplements to submit to FDA reports of serious adverse events associated with the use of dietary supplements. As an AHPA member, NVE supports this effort. However, NVE also respectfully submits that, until such time as FDA can establish a policy that places dietary supplement AER reports submitted to it on an even playing field with AERs related to the OTC drug industry generally, we do not believe that reporting should be mandatory.

FDA should make a determination whether all such reports will be treated as confidential or not. We believe that any system that treats AERs for dietary supplements as publicly available while maintaining confidentiality for such reports for OTC products should be considered arbitrary and capricious. Moreover, in light of FDA's gross mishandling of AERs associated with ephedra products, the wisdom of submitting any such reports to the Agency must be called into question until FDA corrects its approach to these reports.

NVE has provided us with the following information in response to the specific questions you raised:

1. Identify all products that you have manufactured, produced or sold that contain ephedra. For each product identified, provide the following information:
   a. The name of the product;
   b. The date the product was first available for public consumption;
   c. Whether the product is still available for public consumption;
   d. If the answer to Question 1(c) is no, explain when it was taken off the market and your reasons for removing it;
   e. Whether you have developed an "ephedra-free" alternative and, if so, the name of the alternative product and the date it was/will be first available for public consumption; and
   f. The demographics of the target market identified by your company's research (including marketing research performed by non-affiliated companies).

Response:

a-e. See Exhibit 1 attached hereto.

2. State whether you have received consumer complaints or notifications concerning adverse health events associated with any products identified in Question 1. If so, for each year beginning when your product was first available for consumption, provide the following information:
   a. The name of complainant;
   b. The date of complaint;
   c. A summary of consumer's adverse event(s);
   d. A summary of company's response to complaint;
   e. Whether any information about the complaint was reported to the FDA or any other government entity, and if so, a summary of the information that you provided; and
   f. All records relating to such complaints.

Response:

Yes. NVE has no records of consumer complaints before October of 1999.

a. Because of privacy concerns, the names and street addresses of the complainants have been omitted.

b-d. See Exhibits 2 (Customer Adverse Reaction/General Complaint Log) and 3 (Adverse Reaction/Return Log), attached hereto. The Customer Adverse Reaction/General Complaint Log is the general record of customer complaints in connection with adverse reactions to or dissatisfied experiences with NVE's products. The Adverse Reaction/Return Log is a record of product returns from customers who purchase NVE's products directly from NVE, during which the customer is asked to supply a reason for the return.

e. No. There was no requirement to do so.

f. See Exhibit 4 [raw (handwritten) notes and documents] attached hereto.

3. State whether your company has reporting or tracking procedures for adverse health events reported by consumers of your products. If so, identify the entities to which these reports are made, the individual(s) responsible for retaining such information, and describe the specific procedures. Provide a copy of all procedures in this question.

Response:

Upon receipt of a telephone call from a customer inquiring about or complaining of an adverse reaction that the customer believes is related to one of our products, the call is forwarded to the customer service department where the [illegible] advised to discontinue the use of the product immediately, and to seek medical attention, if necessary. The information reported by the customer is [illegible] customer service person is trained

to not attempt to diagnose a medical condition.

If the telephone call (inquiry about a suspected adverse reaction or abuse of one of NVE's products) is from a health or medical care provider or poison control person, the call is forwarded to NVE's Operations Supervisor. The Operations Supervisor attempts to identify the entity through fax of its letterhead or other document. Upon receipt of satisfactory identification (usually done while the caller remains on the telephone, depending upon the urgency) the Operations Supervisor discloses product information such as the active ingredients (which are disclosed on NVE's labels). This information, too, is recorded in NVE's customer tracking system records.

Written complaints of a claimed or suspected adverse reaction to NVE's products have been referred to several persons at NVE in the past, and handled as deemed appropriate under the individual circumstances. Such complaints are now referred to one or more of the following for evaluation and appropriate response: the President or his Administrative Assistant, the General Counsel or his Legal Assistant.

4. State whether a customer has filed any lawsuits against your company alleging health-related problems associated with taking any of the ephedra-containing products identified in Question 1. If so, provide the following information:
   a. The name of the product(s);
   b. The name of the complainant(s);
   c. The date the lawsuit was filed;
   d. A summary of health-related allegations of lawsuit; and
   e. The status of the lawsuit (i.e., pending, settled, verdict).

Response:

See Exhibit 5 attached hereto.

5. Identify all studies or reports (whether or not published) that relate to any ephedra-containing products identified in Question 1. For each such study or report, provide the following information:
   a. The name of the author(s) and/or physician(s) that participated in such study;
   b. The number of participants in the study or report;
   c. Whether you provided any compensation or benefit, monetary or otherwise, to any participant in the study or report;
   d. Whether you provided such compensation or benefit, monetary or otherwise, to any physician associated with the study or report;

e. Whether you commissioned the study or report or contributed any monies to the research associated with the study report; and
f. A copy of all studies or reports identified.

Response:

See Comments of NVE Pharmaceuticals on the Proposed Rule for Dietary Supplements Containing Ephedra Alkaloids dated April 7, 2003 ("white paper") submitted on behalf of NVE by Ullman Shapiro Ullman, LLP to the U. S. Department of Health and Human Services Food and Drug Administration.

6. All records relating to the safety and/or health effects of ephedra supplements, including, but not limited to, records concerning the safety and/or health effects of your ephedra-containing products identified in Question 1.

Response:

To the extent that we understand this question, see NVE's white paper and *Ephedra and Ephedrine for weight loss and Athletic Performance Enhancement: Clinical Efficacy and Side Effects*, Evidence Report/Technology Assessment No. 76 (Prepared by Southern California Evidence-based Practice Center, RAND, under Contract No. 290-97-0001, Task Order No. 9). AHRQ Publication No. 03-E022. Rockville, MD: Agency for Healthcare Research and Quality (February 2003.)

7. Identify who is responsible for determining the dosage that consumers are directed to take for each ephedra-containing product identified in Question 1. Include in your response the person(s) name, the entity with which the person is affiliated, the person's title, and a description of the process by which your company determined the product dosage.

Response:

Robert Occhifinto, President of NVE Pharmaceuticals. Dosages for NVE's ephedra-containing products are based upon the monograph for OTC products that are published in the Code of Federal Regulations.

8. State whether your company is aware of any adverse health-related consequences that may occur if the recommended dosage of any ephedra-containing products identified in Question 1 is exceeded. If so, summarize how you have been made aware of these adverse health effects, and provide all records relating to potential adverse health effects that can occur if the daily dosage is higher than what is recommended on the product label.

Response:

A claimant: Attached hereto collectively as Exhibit 6 are copies of his correspondence and medical records that indicate that he took 4 Black Beauty capsules within hours, without a meal, contrary to the label warning.

A plaintiff, Anthony Clark: Attached as Exhibit 7 are copies of his complaint and his medical records which indicate that he took 25 Yellow Jackets at one time and subsequently died.

9. From the inception of your company to the present, state the company's overall annual revenue and the amount of revenue per year generated from sales of ephedra-containing products. For each such ephedra-containing product identified in Question 1, provide the total revenue per year, per product.

Response:

Attached hereto as Exhibit 8 is a copy of a letter from NVE's Certified Public Accountants detailing NVE's annual revenues from 1994 – 2001. Also, attached hereto as Exhibit 9 is a copy of NVE's sales reports from its earliest available records in late 1999 to the present. As this is a privately held company, these documents are of course, highly confidential. However, they are being submitted in the spirit of cooperation. Notwithstanding this submission, NVE respectfully requests that this information be kept confidential.

10. State the reason for your decision to manufacture "ephedra-free" products and whether the decision to develop "ephedra-free" products was the result of concerns about the adverse health-related effects of supplements containing ephedra.

Response:

No. NVE first manufactured its ephedra-free product in September of 2001 to expand it's market by offering consumers an alternative to ephedra-containing products. NVE still manufactures and distributes ephedra-containing products.

11. All records relating to the development and manufacture of your "ephedra-free" products through the use of ingredients other than ephedra.

Response:

NVE developed Stacker 2 Ephedra Free by substituting Citrus Aurantium for the ephedra. There are no records relating to the development of Stacker 2 Ephedra Free.

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12. State whether you manufacture and sell the product known as "Yellow Jackets." If not, provide the date upon which you ceased manufacture and sale of "Yellow Jackets," the reason(s) for your decision to cease manufacturing and/or selling the product, and explain why the product is still available for public consumption on certain websites, such as www.superiorsupplements.com.

Response:

See response to Question 1. Perhaps other retailers and or distributors have not exhausted their inventories.

13. For each year from 1995 through the present, identify and describe all investigations by state or Federal agencies of your company relating to your products. Include in your response the identity of the investigating agency; the nature of the investigation; and, if applicable, the resolution of the investigation.

Response:

In responding to this question, NVE has construed the word "investigations" broadly to include FDA inspections. See Exhibit 10 attached hereto.

Please note we are informed that many of NVE's responses to the committee's questions come directly from the Exhibits referenced herein. We are further informed that all such Exhibits will be delivered to the committee directly by NVE under a separate cover no later than 5:00 P.M. on May 7, 2003. If you have additional questions please direct them to the undersigned.

Very truly yours,

Ullman, Shapiro, Ullman, LLP

Marc S. Ullman

cc: Hon. John Dingell (by regular mail)
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